

voir can comprise a surface comprising channels or troughs. The Reservoir Bottom can serve to seal Reservoir channels and provides access holes (vias) to the attached chip. FIG. 7 shows top and bottom views of the assembled Fluidic Manifold. The chip can be attached to the bottom surface of the Fluidic Manifold with laser-cut pressure sensitive adhesive. The four Incubation Channels, fed from chip Out1 and Out2 wells on one (proximal) side, can also connect to additional pneumatic lines (or pneumatic channels) via Pneumatic Inserts (FIG. 5), on their other (distal) sides. The pneumatic inserts can provide for distal side connections that can allow air to escape or enter the incubation channels (which may be serpentine channels) as they are filled and emptied, respectively. Alternatively, they can be used to supply positive pressure or vacuum to the channels. Channel cross-sections can be 0.5 mm deep×1 mm wide, and channel length is approximately 200 mm (about 100 ul volume). In addition to Incubation Channels, the Fluidic Manifold can also contain Reagent Storage Channels. These can be filled from wells on the top surface of the Fluidic Manifold, and emptied into chip input/output wells. They can be designed to hold reagents at 4C for long periods of time, with minimal evaporation and condensation. Finally, four thermocouple channels can provide temperature measurement points for each of the four Incubation Channels. FIG. 8, FIG. 9, and FIG. 10 shows photographs of a system that lacks reagent Storage Channels. FIG. 8 shows a view of the Fluidic Manifold is resting on Pneumatic Floater (no chip). Heat sink and fan assembly can be visible beneath the Aluminum Manifold. FIG. 9 shows a top view of wells and incubation serpentine channels above copper heat spreader plates (on top of TECs) are shown. Two thermocouple wires leaving the assembly are visible. FIG. 10 shows an Aluminum Manifold and Pneumatic Floater. Copper heat spreading plates on top of TEC's, and Pneumatic Floater o-rings are visible.

[0074] A cartridge can be constructed of any material known to those skilled in the art. For example, the cartridge can be constructed of a plastic, glass, or metal. A plastic material may include any plastic known to those skilled in the art, such as polypropylene, polystyrene, polyethylene, polyethylene terephthalate, polyester, polyamide, poly(vinylchloride), polycarbonate, polyurethane, polyvinylidene chloride, cyclic olefin copolymer (COC), or any combination thereof. The cartridge can be formed using any technique known to those skilled in the art, such as soft-lithography, hard-lithography, milling, embossing, ablating, drilling, etching, injection molding, or any combination thereof.

[0075] In some embodiments of the invention, a smooth fluidic manifold, or smooth components can be formed by injection molding. Additionally, adhesive and thermal bonding methods can be used for assembly. Use of smooth surfaces and/or certain types of materials, e.g., cyclic olefin copolymer, can reduce the formation of bubbles during heating steps. In some embodiments, materials that have low liquid and/or gas adsorption or absorption can be chosen. In other embodiments, materials that exhibit rigidity or low temperature dependent mechanical deformation can be chosen.

[0076] As shown in FIG. 11, the Fluidic Manifold can comprise three pieces: Cap, Channel Manifold, and Bottom (not visible). Injection molding fabrication can provide smooth channel surfaces. Adhesive and thermal bonding methods can be used for assembly. Preliminary evaluation of this system shows that it remains bubble-free up to approximately 95C. The left-hand portion of FIG. 11 shows a modi-

fied fluidic reservoir with aluminum bezel for enhanced mechanical stability. The right-hand portion of FIG. 11 shows a three piece fluidic manifold. Injection molded COC channel manifold and machined polycarbonate cap (carrying input/output wells) are visible.

[0077] FIG. 12 shows the structure of the Fluidic Manifold in more detail. Thermocouples can be replaced with small thermistors that may eliminate the requirement for direct wiring to the FTC100 temperature controller, and the associated flying leads. Instead, electrical connections can be made via contact pads on the bottom surface of the Fluidic Manifold and matching pogo pins in the Aluminum Manifold. The left-hand portion of FIG. 12 shows an exploded view of the three piece structure where the Bottom sealing the Channel Manifold is clearly visible. The middle and right-hand portion of FIG. 12 show top and bottom views. Wells in Cap, and features on the bottom surface of the Channel Manifold are clearly visible.

B. Microfluidic Chips

[0078] In some instances, the microfluidic chip has diaphragm valves for the control of fluid flow. Microfluidic devices with diaphragm valves that control fluid flow have been described in U.S. Pat. No. 7,445,926, U.S. Patent Publication Nos. 2006/0073484, 2006/0073484, 2007/0248958, and 2008/0014576, and PCT Publication No. WO 2008/115626, which are hereby incorporated by reference in their entirety. The valves can be controlled by applying positive or negative pressure to a pneumatics layer of the microchip through a pneumatic manifold.

[0079] In one embodiment, the microchip is a "MOVE" chip. Such chips comprise three functional layers—a fluidics layer that comprises microfluidic channels; a pneumatics layer that comprises pneumatics channels and an actuation layer sandwiched between the two other layers. In certain embodiments, the fluidics layer is comprised of two layers. One layer can comprise grooves that provide the microfluidics channels, and vias, or holes that pass from the outside surface to a fluidics channel. A second layer can comprise vias that pass from a surface that is in contact with the actuation layer to the surface in contact with the pneumatic channels on the other layer. When contacted together, these two layers form a single fluidics layer that comprises internal channels and vias that open out to connect a channel with the fluidics manifold or in to connect a channel with the activation layer, to form a valve, chamber or other functional item. The actuation layer typically is formed of an elastomeric substance that can deform when vacuum or pressure is exerted on it. At points where the fluidic channels or pneumatic channels open onto or are otherwise in contact with the actuation layer, functional devices such as valves can be formed. Such a valve is depicted in cross section in FIG. 15. Both the fluidics layer and the pneumatics layer can comprise ports that connect channels to the outside surface as ports. Such ports can be adapted to engage fluidics manifolds, e.g., cartridges, or pneumatics manifolds.

[0080] As shown in FIG. 1, the microfluidic chip (103) can be interfaced with the cartridge (101). The microfluidic chip can have a chamber (105) with an opening that is mated to an opening (117) of the cartridge (101). The chamber can be used for a variety of purposes. For example, the chamber can be used as a reaction chamber, a mixing chamber, or a capture chamber. The chamber can be used to capture magnetic par-